Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Response to advances statistical methods and designs for clinical trials for COVID-19 ☆

We agree with colleagues that the use of the chi-squared and one-sided Fisher tests to compare PCR-negative rates in our study were possibly not the best appropriate tests, given the small sample sizes [1]. The proposed alternative tests (Barnard and Wang tests) give a much higher statistical power. Interestingly, these tests confirmed the effectiveness of hydroxychloroquine (HCQ). We also agree that excluding six patients from our analysis may have biased the results. For that reason, we reanalyzed our data on the 42 patients initially enrolled in our survey, including those transferred to intensive care unit. The p-value was calculated using Barnard exact unconditional test and confidence intervals (95%CI) were estimated using the Wang exact 95% one-sided lower limit, as proposed. Statistical analysis was conducted using R [R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, 2020. URL: https://www.Rproject.org/].

Table 1 shows our updated results. The positive 95% CI confirmed the effectiveness of HCQ as did the Barnard test and it concluded that the use of HCQ increased the PCR-negative rate by at least 50.6% with 95% confidence.

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Ethical approval

Not applicable.

Declaration of Competing Interest

The authors declare no competing interests.

Reference

[1] Dos Santos MR, Referring to the study: Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open label non-randomized clinical trial. Int J Antimicrob Agents 2021: 106176.

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Table 1
Proportion differences of PCR negative patients in the hydroxychloroquine group and the control group.

	Day 3[23,18]	Day 4[22,18]	Day 5[22,18]	Day 6[22,18]	Day 7[22,14]
Hydroxychloroquine treatment	43.5%	54.6%	59.1%	63.6%	59.1%
Control patients	11.1%	27.8%	22.2%	16.7%	28.6%
Proportion difference	32.4%	26.8%	36.9%	46.9%	30.5%
Barnard one-sided p-value	0.0133	0.0515	0.0109	0.0014	0.0572
Wang one-sided confidence interval	[54.8%, 1]	[51.2%, 1]	[56.7%, 1]	[63.1%, 1]	[50.6%, 1]

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